Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Asian Journal of Psychiatry 73 (2022) 103123

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Letter to the Editor

First episode psychosis and COVID-19: A case series and mini review

ARTICLE INFO

Keywords
Psychosis
COVID and Psychosis
COVID induced psychosis
Psychosis in COVID-19 patients

1. Introduction

Since the pandemic, there has been an increase in psychiatric morbidity among the individuals infected and those impacted indirectly due to the COVID 19. There is a significant rise in psychiatric illnesses like anxiety, depression, acute stress disorders, adjustment, and PTSD (Rogers et al., 2020). The causative factors implicated include psychological factors such as stress due to fear of infection and death, social isolation, uncertainty about the future, and neurobiological factors like Inflammatory markers and cytokines (Dubey et al., 2020). Drugs such as steroids and hydroxychloroquine have also precipitated psychiatric disorders such as mania and psychosis (Correa-Palacio et al., 2020).

Brown et al. reviewed literature from H1N1 influenza, Ebola, SARS, Middle East Respiratory Syndrome (MERS), and COVID-19 outbreaks. They estimated that 0.9–4% of people exposed to a virus during an epi- or pandemic developed psychosis or psychotic symptoms, significantly higher than the median incidence rate of.015% for psychosis in the general population, further emphasizing the direct role of viral infections as an independent risk factor leading to Psychiatric disorders especially psychosis (Brown et al., 2020).

In this case series, we discuss the COVID-19 'physically' asymptomatic patients who developed first episode psychosis without any prior risk for psychiatric disorders highlighting the direct role of COVID-19 inflammatory response and psychological distress in psychosis causation.

2. Narrative

2.1. Case-1

Ms. D, is a 36-year-old woman, with no past /family history of psychiatric disorders. Her mother-in-law had tested positive for COVID-19, Real-time Reverse Transcriptase Polymerase chain reaction (RTPCR), following which she developed an intense fear of catching COVID-19. Two days after her Mother-in-law turned positive, she started developing Fever, with no other symptoms of Influenza-like illness (ILI). She consulted a General Physician and was functioning well. On day-4, she started to hear voices, suspiciousness, reduced oral intake, outbursts of anger and inappropriate laughter. She came to our Emergency Department (ED) with this history and upon evaluation she had abrupt onset of disorganized speech, ideas of persecution, auditory hallucinations and features of Catatonia (Bush Francis Catatonia Rating scale showed a score of 7 on admission) like excitement, withdrawal, and negativism. She was diagnosed with Acute and Transient Psychotic Disorder (ATPD). COVID 19 positive status was confirmed and she was admitted in COVID-19 designated ward. She was started on concurrent treatment of COVID protocol prevailing at that time (methylprednisolone, doxycycline, and vitamin supplements according to protocol (Navin et al., 2021). Psychotropics were initiated, Olanzapine 10 mg HS for psychotic symptoms, and Lorazepam (2 mg TID) for Catatonia.

3 days post in-patient care she developed, ILI symptoms of Myalgia and mild fever (99.4 F). Subsequently she developed Tachycardia (with T-wave inversion) and Hypertension (Day 8 of COVID positive status), for which she was treated with Metoprolol (25 mg BD). By 7 days post admission, her BFCRS reduced to 2, and her clinical symptoms including psychopathology reduced in their severity. During the course of IP care, she received supportive care and monitoring, she did not receive steroids or any other antiviral drugs.

Investigations: At the start of In-patient care (day 4 of RTPCR Positive): baseline: CRP: 3, D-Dimers: 270, NLR: 1.4; inflammatory markers-LDH, CRP, Ferritin, D-Dimer were monitored every 3 days, along with Hemogram, Liver, Renal function tests, and Serum electrolytes which were normal at baseline. There was a spike in NLR on Day 6 of illness (3.6), which decreased gradually over the next 4 days. There was also a spike in CRP (19), and D-Dimers (527) on day 8 of illness, but they too had reached within normal limits by day 10 of illness (CRP 5 mg/L, Ferritin 56 mcg/L, LDH 186 mcg/L, NLR 2.0, ALP 63 mcg/L).

After her ILI symptoms improved and her inflammatory markers normalized, RTPCR was repeated (on Day 14), which was negative, and the patient was shifted to a general ward for the management of persistent psychotic symptoms (2nd and 3rd person auditory hallucinations). She showed improvement in psychotic symptoms within the next 1 week, however, anxious ruminations persisted at discharge.

https://doi.org/10.1016/j.ajp.2022.103123
Received 15 March 2022; Accepted 7 April 2022
Available online 14 April 2022

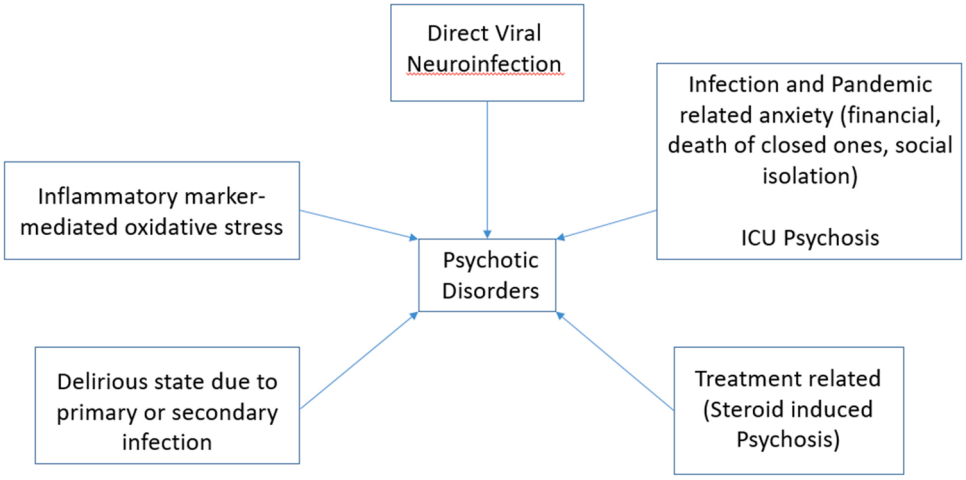

Fig. 1. Etiological pathways of COVID infections and development of psychosis.

2.2. Case 2

Mr. J, 29-year-old male, with no past history of psychiatric illness presented to our ED, with abrupt onset illness of 3 days duration with symptoms characterized by sleep disturbances, abnormal behavior, incomprehensible speech, crying spells, unexplained irritability and anger outbursts, including attempts to harm self and others. Upon evaluation, he was agitated, had delusions of persecution, delusions of reference, muttering to self, dysphoric affect, and suicidal ideations. A provisional diagnosis of ATPD was made.

On routine risk assessment for COVID 19 infection, his family reported that he got exposed to his brother who was COVID-19 positive couple of weeks ago. The patient had no symptoms of COVID-19. But tested positive on RT-PCR test for COVID-19. He was then admitted in COVID-19 designated ward for management of both asymptomatic COVID-19 and psychosis. As per our protocol for management of COVID-19, he was started on Ivermectin, Doxycycline and Vitamin supplementation, and he remained asymptomatic for ILI symptoms throughout his stay in the hospital.

He was started on Risperidone up to 6 mg, Trihexyphenidyl up to 2 mg and Clonazepam SOS being used for sleep occasionally. Improvement was noted in all Psychotic symptoms and reached premorbid level in 3 days. He was discharged on 6th day of admission and was advised home quarantine for 14 days after discharge.

Investigations: Inflammatory markers and Neutrophil-lymphocyte ratio were elevated (LDH was 273, Ferritin was 202, CRP was 14, D-Dimer was 554) at the time of admission, which had normalized over 6 days of illness onset. Patient again visited ED after one month, despite being on regular medications, he relapsed with similar set of psychotic symptoms. Patient tested negative for COVID-19 on RTPCR during this time and was treated on OPD basis with T. olanzapine.

3. Discussion

There is a need to understand the role of psychological distress before solely attributing new onset psychiatric symptoms to mere biological changes or medication usage in COVID infection. Huarcaya-Victoria et al., in their report mentioned, a patient developed anxiety severe enough to produce psychotic symptoms despite mild-moderate COVID-19 (Huarcaya-Victoria et al., 2020), giving more credence to the coining of the term "Coronaphobia" (Asmundson and Taylor, 2020), which is almost similar to the first case described in this report. Our patient did not have any significant family or past history of psychiatric disorders, but developed significant fear and anxiety about contracting COVID-19 infection subsequently developing persecutory delusions. Also, the inflammatory markers and blood reports were normal at the time of onset of the psychosis which says that the psychological distress could be the sole contributing factor for the first episode psychosis.

Jonathan et al., in his meta-analysis emphasized the role of psychological distress in COVID-19 patients leading to various psychiatric disorders like anxiety, Confusion and affective disorders (Rogers et al., 2020). Chacko described that emergence of psychiatric symptoms does not always depend on the severity of COVID-19 infection (Chacko et al., 2020). In the first case, her inflammatory markers were marginally raised, and only for first 2 days of illness. So psychological factors, mainly anxiety regarding spread of COVID-19, is arguably the most reasonable explanation for her symptoms. In the case series described here too had only mild ILI symptoms like myalgia and low-grade fever.

In Case-2, though there was COVID 19 infection in the family, the patient had functioned well until the onset of psychiatric symptoms. He did not actively express any stress or fear of contacting COVID-19 infection unlike Case-1. He did not have any past or family history of psychiatric illness either. So, we must consider the role of biochemical mediators of infection and viremic status as possible etiological agents for psychiatric symptom development. There has been evidence of raised Inflammatory markers, including CRP, TNF alpha and IL-6, that have been linked with psychosis not only in COVID-19, but also in other Coronaviral and other infections (Chacko et al., 2020). CRP, LDH, D-Dimer, Ferritin, and NLR were elevated initially, and within a week all the biological parameters reached normal values and the psychopathology improved which emphasizes the direct relation between the psychiatric symptoms and inflammatory markers. So, his acute phase reactants profile can be considered to have played a role in psychiatric illness origin. Monitoring IL-6 was logistically not feasible for us due to varying results with sample collection time and testing. But, raised IL6 is frequently found in COVID-19 infection and has been linked in the past with the development of first episode psychosis (Ferrando et al., 2020a). However, relapse of symptoms was also noted in case-2 post COVID-19 infection reminding us of the possible long-term effects of COVID-19 infection and need for longitudinal research in this area. Taquet et al., 2021 has also highlighted the possibilities of neurological and psychiatric symptom till six months post COVID infection. In this study, the hazard ratio (HR) for the psychotic disorder was greater in patients with hospitalization compared with those without (Taquet et al., 2021). This suggests that the more severe the infection, the higher the risk of neuropsychiatric symptoms which is similar to case-2.

In this case series we highlight how asymptomatic and mildly symptomatic individuals with COVID-19 symptoms can develop severe psychosis requiring hospitalization. There are reports indicating how COVID-19 individuals with severe ILI symptoms can develop psychosis, however, in the above cases we highlight new onset psychosis in COVID-19 asymptomatic patients. In Fig. 1 we extrapolate the possible

etiological pathways of COVID infections and development of Psychiatric Illness, psychotic disorders in particular.

Role of funding source

None. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

None.

Conflict of Interest

None.

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P. Lakshmi Nirisha, Aandi Subramaniyam Bhaskaran, Naveen Achyuta Yedavally, Hari Hara Suchandra *, Narayana Manjunatha, Chennaveerachari Naveen Kumar, Suresh Bada Math

Department of Psychiatry, National Institute of Mental Health and Neuro Sciences, Bangalore 560029, India

* Corresponding author.
E-mail address: suchikhhr02@gmail.com (H.H. Suchandra).